REMARKS

Claims 1-125 are pending. Claims 20-37 and 46-125 are withdrawn as directed to non-elected claims. Claims 2-5 and 7-10 are canceled herein. New claims 126-128 have been added, support for which can be found in the specification at least at page 19, lines 3-18. Thus, claims 1, 6, 11-19, 38-45, and 126-128 are under consideration. Claims 1, 6, 11-18, and 38 are amended herein. Support for claim 1 can be found in the specification at least at page 15, lines 5-27. Claims 11-18 and 38 were amended to depend from claim 1 and to correct antecedent basis. It is believed that no new matter is entered by way of these amendments.

Applicants respectfully acknowledge the withdrawal of the rejections of claims 1-19 and 38-45 under 35 U.S.C. § 112, first paragraph and the withdrawal of the rejections of claims 1-5, 18-19, 38, and 42 under 35 U.S.C. § 102(b).

35 U.S.C. § 102

Claims 1-19, 38, and 42 remain rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by WO 02/077021 ("Masignani"). Claims 2-5 and 7-10 are canceled herein rendering rejection of these claims moot. Applicants respectfully traverse this rejection with respect to the remaining claims.

Claim 1 recites an isolated detoxified pneumococcal neuraminidase or portion thereof comprising an amino acid sequence of a non-detoxified neuraminidase with at least one amino acid substitution, wherein the detoxified pneumococcal neuraminidase or portion thereof has reduced activity as compared to the non-detoxified neuraminidase and wherein the detoxified pneumococcal neuraminidase or portion thereof is antigenic. Claim 6 recites that the isolated detoxified pneumococcal neuraminidase or portion thereof of claim 1 comprises a deletion of at least 7% of the naturally occurring amino acids of a non-detoxified neuraminidase. Claims 11-13 recite that the isolated detoxified pneumococcal neuraminidase or portion thereof of claim 1 comprises a deletion of at least 5, 10, and 15 N-terminal amino acids of the non-detoxified neuraminidase, respectively. Claims 14-17 recite that the isolated detoxified pneumococcal neuraminidase or portion thereof of claim 1 comprises a deletion of at least 10%, 20%, 30%, and 35% of the C-terminal amino acids of the non-detoxified neuraminidase, respectively. Claim 18 recites a composition comprising the isolated detoxified pneumococcal neuraminidase or portion

thereof of claim 1 and a pharmaceutically acceptable carrier. Claim 19 recites the composition of claim 18, further comprising an adjuvant. Claim 38 recites a composition comprising the isolated detoxified pneumococcal neuraminidase or portion thereof of claim 1 and a pharmaceutically acceptable carrier, wherein the composition is suitable for administration to a mucosal surface. Claim 42 recites a container comprising the composition of claim 38.

The Examiner, at page 3 of the Office Action, states,

> "Applicants are again directed to the teachings of Masignani, specifically, claim 3, which recites a 'protein comprising a **fragment** of an amino acid sequence selected from the group consisting of...' Masignani et al further define such fragments to include 7 or more consecutive amino acids starting from the N-terminus (e.g., 8, 10, 12, 14, 16, 18, 20, 30, 40, 50, 60, 70, 80, 90, 100 or more). (See page 1). Given that neuraminidase is a protein identified in claim 3, every single one of the above described fragments would be structurally identical to the structural requirements set forth in the claims. For example, Applicants specification (page 15, lines 12-13 sets forth that 'amino acid residues 383-387, 467-473, 541-546, or 610-616' can be substituted, **deleted**, or altered to create a detoxified pneumococcal neuraminidase. Every single one of the 'fragments' disclosed by Masignani (7, 8, 10, 12, 14, 16, 18, 20, 30, 40, 50, 60, 70, 80, 90, 100 consecutive amino acids) starting from the N-terminus would lack amino acids 383-387, 467-473, 541-546, and 610-616. Accordingly, the structure described by Masignani is identical to the structural requirements set forth in the instant claims."

Applicants note claim 1, as amended, recites that the isolated detoxified pneumococcal neuraminidase or portion thereof comprising an amino acid sequence of a non-detoxified neuraminidase ***with at least one amino acid substitution***, wherein the detoxified pneumococcal neuraminidase or portion thereof has reduced activity as compared to the non-detoxified neuraminidase and wherein the detoxified pneumococcal neuraminidase or portion thereof is antigenic. Masignani discloses fragments of amino acid sequences from *Streptococcus pneumonia*, including a neuraminidase, wherein the fragments include 7 or more consecutive amino acids starting from the N-terminus, as stated above by the Examiner. However,

Masignani fails to disclose or suggest an isolated detoxified pneumococcal neuraminidase or portion thereof comprising an amino acid sequence of a non-detoxified neuraminidase ***with at least one amino acid substitution***. Applicants note, "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Masignani fails to disclose each and every element of claim 1, thus Masignani fails to anticipate claim 1. Claims 6, 11-19, 38 and 42 depend directly or indirectly from claim 1, and, thus, include each and every element of claim 1, as amended. Therefore, Masignani fails to anticipate claims 1, 6, 11-19, 38, and 42.

Further, Masignani does not enable one of skill in the art to produce an isolated detoxified pneumococcal neuraminidase or portion thereof comprising an amino acid sequence of a non-detoxified neuraminidase with at least one amino acid substitution, wherein the detoxified pneumococcal neuraminidase or portion thereof has reduced activity as compared to the non-detoxified neuraminidase and wherein the detoxified pneumococcal neuraminidase or portion thereof is antigenic. The specification, at page 15, lines 5-6, defines detoxification by stating, "'detoxification' is meant a reduction or elimination in enzymatic activity, while maintaining antigenicity or immunogenicity." Masignani fails to disclose or suggest ways to determine whether the enzymatic activity of the neuraminidase fragments has been reduced or eliminated and further fails to disclose or suggest how to determine antigenicity and immunogenicity. Therefore, Masignani does not anticipate claims 1, 6, 11-19, 38, and 42, at least because Masignani is not enabling and fails to disclose or suggest each and every element of the claims. Thus, claims 1, 6, 11-19, 38, and 42 are novel. Applicants respectfully request reconsideration and withdrawal of this rejection.

35 U.S.C. § 103

Claims 1-19 and 38-45 remain rejected under 35 U.S.C. § 103(a) for allegedly being obvious based on Masignani in view of U.S. Patent No. 7,202,056 ("Lee"). Claims 2-5 and 7-10 are canceled herein rendering rejection of these claims moot. Applicants respectfully traverse this rejection with respect to the remaining claims.

Masignani and Lee, alone and in combination, fail to disclose or suggest an isolated detoxified pneumococcal neuraminidase or portion thereof comprising an amino acid sequence of a non-detoxified neuraminidase ***with at least one amino acid substitution***, wherein the detoxified pneumococcal neuraminidase or portion thereof has reduced activity as compared to the non-detoxified neuraminidase and wherein the detoxified pneumococcal neuraminidase or portion thereof is antigenic. As stated above, Masignani fails to disclose or suggest an isolated detoxified pneumococcal neuraminidase or portion thereof comprising an amino acid sequence of a non-detoxified neuraminidase ***with at least one amino acid substitution***, compositions comprising the same isolated detoxified pneumococcal neuraminidases or portions thereof and a pharmaceutically acceptable carrier; the same compositions suitable for administration to a mucosal surface; and containers comprising these compositions. Lee and those of skill in the art fail to make up for this deficiency. Lee is directed to polynucleotides encoding BGS-19 polypeptides, fragments and homologues thereof and methods for applying the novel BGS-19 polypeptides to the diagnosis, treatment, and/or prevention of various diseases (see abstract). However, Lee fails to disclose or suggest an isolated detoxified pneumococcal neuraminidase, let alone an isolated detoxified pneumococcal neuraminidase or portion thereof comprising an amino acid sequence of a non-detoxified neuraminidase ***with at least one amino acid substitution***. Thus, Lee fails to make up for the deficiencies of Masignani. Therefore, the cited references, alone and in combination, fail to disclose or suggest each and every element of the claims.

Further, Masignani and Lee, alone or in combination, fail to provide one of skill in the art with a reasonable expectation of success. Applicants note that references relied upon to support a rejection under 35 U.S.C. § 103 must provide an enabling disclosure, i.e., "they must place the claimed invention in the possession of the public." See *Beckman Instruments, Inc. v. LKB Produkter AB*, 12 USPQ2d 1301 (Fed. Cir. 1989). Masignani and Lee, individually and in combination, fail to provide an enabling disclosure, and, thus, a reasonable expectation of success. This is because Masignani and Lee, as stated above, fail to disclose or suggest an isolated detoxified pneumococcal neuraminidase or portion thereof comprising an amino acid sequence of non-detoxified neuraminidase ***with at least one amino acid substitution***, wherein the detoxified pneumococcal neuraminidase or portion thereof has reduced activity as compared

to the non-detoxified neuraminidase and wherein the detoxified pneumococcal neuraminidase or portion thereof is antigenic. Further, Masignani and Lee, alone and in combination, by definition, fail to disclose or suggest ways to determine whether the pneumococcal neuraminidase is detoxified. Specifically, Masignani and Lee, fail to disclose or suggest ways to determine whether the enzymatic activity of the neuraminidase fragments has been reduced or eliminated. Masignani and Lee, alone and in combination, additionally fail to disclose or suggest ways to determine whether the detoxified neuraminidase or portion thereof maintains antigenicity or immunogenicity. Therefore, Masignani and Lee fail to disclose or suggest an isolated detoxified pneumococcal neuraminidase or portion thereof comprising an amino acid sequence of non-detoxified neuraminidase ***with at least one amino acid substitution***; compositions comprising the same isolated detoxified pneumococcal neuraminidase or portion thereof and a pharmaceutically acceptable carrier; the same compositions, wherein the compositions are suitable for administration to a mucosal surface; and containers comprising the disclosed compositions. Therefore, the cited references, in combination, fail to provide one of skill in the art with a reasonable expectation of success.

Further, as described in the previous response of June 3, 2009, the detoxified pneumococcal neuraminidases claimed in the present application have surprising and unpredictable properties. As described in the specification at page 45, lines 5-16, pneumococci NanA mutants were recovered from tissues, including olfactory bulbs and CNS tissues in far fewer numbers than wildtype pneumococci. These findings demonstrate that nasal carriage is a prerequisite for more invasive disease and that "interventions capable of reducing carriage, ***such as immunization with NanA***, will offer protection against pneumonia, meningitis, otitis-media, and sepsis." See page 45, lines 14-16 of the specification. Further, the abstract enclosed in the response of June 3, 2009, states, "NanA-mediated immune protection against colonization does not require an enzyamtically active neuraminidase." Therefore, there is a technical advantage to using the detoxified pneumococcal neuraminidases to provide immune protection as described in Example 2 of the specification. Tthe isolated detoxified pneumococcal neuraminidases or portions thereof of the present application possess surprising and unpredictable properties not deducible from Masignani, especially since Masignani fails to disclose or suggest an isolated detoxified pneumococcal neuraminidase or any properties of an isolated detoxified

pneumococcal neuraminidase. Lee fails to disclose or suggest an isolated detoxified pneumococcal neuraminidase, and, thus, Lee fails to make up for the deficiencies of Masignani.

In summary, the cited references, alone or in combination, fail to disclose or suggest each and every element of the claims, fail to provide an enabling disclosure, and fail to provide one of skill in the art with a reasonable expectation of success. The skill of those in the art does not make up for these deficiencies. Additionally, the claimed isolated detoxified pneumococcal neuraminidases or antigenic fragments thereof have surprising and unpredictable properties. Therefore, claims 1-19 and 38-45 are not obvious based on Masignani in view of Lee. Applicants respectfully request reconsideration and withdrawal of this rejection.

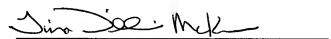
It is believed that all issues raised by the Examiner have been addressed. However, the absence of a reply to a specific rejection, issue, or comment does not signify agreement with or concession of that rejection, issue, or comment. In addition, because the arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed. Finally, the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

Finally, Applicants respectfully call the Examiner's attention to related U.S.S.N. 12/601,233. Applicants encourage the Examiner to review the file history for this matter.

It is believed that no fee is due. However, please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: March 24, 2010



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